[redacted]

INVOICE CHECK LIST

MKULIRA Subproject

At Date of Original Authorization	Period Covered	Time Extended To	Allotment Number	Amount of Obligation
15 Sept 1960				6,500

Additional Authorizations	Period Covered	Time Extended To	Allotment Number	Amount of Obligation
#1				-0-

Invoice Number	Date	Amount	Balance
#1	16 Sept 1960	5073.78 1426.22	-0-
REMARKS:			

[redacted]

MKULTRA, Subproject 124 [redacted]

Purposes: To develop a more sophistica[redacted]
dioxide tension and pH of body fluids; to study relation[redacted]
pH and psychophysiological variables.

Initiated: September 1960

Contractor: [redacted] as a grantee of the [redacted]

Cost: $6,500.00

Status:

[redacted]

12-3

[redacted]

TO: [redacted]

1. Date of Obligation: N/A

2. Purpose of Project: Research in "The Psychophysiological Correlates of Carbon Dioxide Environment"

[redacted]

3. Progress to Date: Project being initiated.

4. Expiration Date: N/A

5. Project Monitor: [redacted]

FROM: [redacted] TSSK D

[redacted]

Room B-10, [redacted] Building, Ext. [redacted]

(When Filled In)

ACCOUNTING BY INDIVIDUAL FOR ADVANCE

NOTE: *Follow Instructions on Reverse*

SUBMITTED BY: MKULTRA, Subproject 124

DATE - VOUCHER NO. 2-12: 652241 MAR 8 66

PERIOD OF ACCOUNTING — FROM: 1 April 1963 — TO: 30 December 1965

1. CASH ON HAND BEGINNING OF PERIOD	$ 2,537.79
2. OUTSTANDING ADVANCES BEGINNING OF PERIOD	
3. RECEIPTS THIS PERIOD:	

RECEIPT NUMBER	DATE	DESCRIPTION
		760.0 25 770185
		# 000124

4. TOTAL TO ACCOUNT FOR	$ 2,537.79

5. EXPENSES THIS PERIOD:

VOUCHER NUMBER	DATE	DESCRIPTION	AMOUNT
		Expense (see attached)	$ 2,497.25
		Refund to [redacted]	
		to be recorded in [redacted]	
		180.0 acct	40.54
		TOTAL EXPENSES	$ 2,537.79

6. REFUNDED HEREWITH — CASH — CHECK — MONEY ORDER	
7. OUTSTANDING ADVANCES END OF PERIOD (Attach listing)	
8. CASH ON HAND END OF PERIOD OR BALANCE DUE ADVANCEE	
9. TOTAL ACCOUNTED FOR	$ 2,537.79

I CERTIFY FUNDS ARE AVAILABLE

OBLIG. REF. NO.	CHARGE FAN ACCOUNT NO.
533	1125-1390-3902
2331	6125-0086 (40.54)

DATE — SIGNATURE OF AUTHORIZING OFFICER

APPROVED — DATE — SIGNATURE OF APPROVING OFFICER: SIDNEY GOTTLIEB, DC/TSD

CERTIFIED FOR PAYMENT OR CREDIT — DATE — SIGNATURE OF CERTIFYING OFFICER

I certify that the expenditures listed hereon and on any attachments were incurred for official purposes of a confidential nature, that payment or credit therefor has not been received, and that this accounting is true and correct.

SIGNATURE OF PAYEE: [redacted]

SPACE BELOW FOR EXCLUSIVE USE OF OFFICE OF FINANCE

DESCRIPTION - ADVANCE ACCOUNTS 13-27	28-33 T/A NO. / SHIP. DOC. NO.	34-39 STATION CODE / REC. RPT. NO. / PROJECT NO.	40-41 EXPEND CODE	42-47 OBLIG. REF. NO. / ADVANCE ACCT. NO. / EMP. NO.	48-49 PAY PER. LIQ. CODE	50 CA DR COST YR.	51-54 GENERAL LEDGER ACCT. NO.	55-66 COST - FAN ACCOUNT SYMBOL / 61-66 CK. NO. X REF. NO.	67-70 OBJECT CLASS / 68-70 DUE DATE	71-80 AMOUNT DEBIT	CREDIT
MKULTRA SUBP 124							199.0			2537.79	
[illegible]	25	770185		124			760.0				2537.79
[redacted] REFUND	25	320177					180.06			40.54	
[redacted]							200.0				40.54
[redacted] REFUND			56	2331		3	610.0	6125-0086	[illegible]	40.54	
[redacted] REFUND			56	533			610.0	1125-1390-3902	[illegible]		40.54
TOTALS										[illegible]	[illegible]

DATE: [illegible] — PREPARED BY: [redacted] — DATE — REVIEWED BY

FORM 4-65 282 OBSOLETE PREVIOUS EDITIONS [redacted] [redacted] (1-49)

[redacted] 124-5

CERTIFICATION

1. This is to certify that I have received an accounting from MKULTRA, Subproject 124 which reflects expenses of $2,497.25. The accounting is being retained in the office of TSD where it may be reviewed by the certifying officer upon request.

2. The balance remaining after recording the expenditures has been refunded. This refund in the amount of $40.54 has been recorded on the [redacted] proprietary company financial records.

3. I certify that satisfactory services represented by the accounting have been received and that to the best of my knowledge and belief the funds expended were for the purposes authorized by the project approval.

[redacted] A

APPROVED:

SIDNEY GOTTLIEB
DC/TSD

[redacted]

[redacted] B

[redacted] B 12X6

[redacted] C

[redacted] C

[redacted] C

Dea[redacted] C

We present herewith the final accounting of the Acid Base Research Project.

Receipts

1960 - October	$3,250.00
1961 - February	3,250.00
	$6,500.00

Disbursements

1960 - Equipment - [redacted]		B	$2,449.16
1960 - Equipment - [redacted]		B	1,300.00
1960 - Other expenditures			213.05
1961 - No disbursements			
1962 - No disbursements			
1963 - 7-16	Labor		158.00
- 8-30	Labor		441.00
- 9-12	Labor		222.00
1964 - 2-18	Labor		208.00
- 9-14	[redacted]	B	25.01
- 11-23	[redacted] Mixing Device		302.93
-111-23	[redacted] Consultant	B	100.00
- 11-23	[redacted] Consultant	B	250.00
- 12-28	[redacted]	B	22.79
- 12-28	[redacted]	B	78.52
1965 - 1-21	[redacted] for advance for subjects, prisoner technicians		600.00
- 2-19	[redacted]	B	60.00
- 4-26	[redacted]	B	29.00
			$6,459.46

Dec. 30, 1965 Balance remaining $ 40.54

Our check in the amount of $40.54, representing the unexpended balance, is enclosed.

Very truly yours,

[redacted] C

124-7

[redacted]

October 8, 1964

[redacted]

Dear Miss [redacted]

I have just received a statement from Mr [redacted] Controller, [redacted] regarding the balance in our Acid Base Project. Mr [redacted] has been away on vacation and this explains the delay.

The amount remaining in the fund is $1,508.78.

Of the approximately $1,000 expended since our last report, over 95% has gone for payroll.

At the present time we are engaged in a study in which the background knowledge and apparatus provided in the grant will be of considerable use. We are administering carbon dioxide and air in mixtures up to 10% carbon dioxide to hypertensive prisoner subjects in an attempt to study the effect on resting blood pressure level. That the acid base level is related to the resting rate of blood pressure is a long-shot hypothesis. If any effect is demonstrated, this could be an important contribution. We plan to measure changes in the acid base balance and blood pressure and particularly the length of time that these changes persist. There is some evidence in the literature that if one sets carbon dioxide tolerance at a new level, that homeostatic mechanisms will maintain this for a considerable period of time. I will certainly keep you informed of our results in this experiment.

I certify that services or materials have been satisfactorily received and the expenditures were incurred on official business.

Sincerely,

[redacted]

[redacted]

Date: 27 OCT 1964

DOES NOT CONSIDER THIS AN ACCTG. MERELY A STATEMENT

[redacted]

124-8

September 10, 1963

[redacted]

Dear [redacted]

Pursuant to my letter of April 25, I am reporting to you on the Acid-Base Study. During the past two months we have trained a technician to work with th[redacted]pparatus. He will be a student in Chemistry this fall at th[redacted] We expect to run experimental subjects on week-ends.

We attempted one experiment to simplify finger blood collection by catching it under oil. This failed because of oil contamination of the electrode. Therefore we will proceed with subjects according to standard [redacted]ethods.

Funds remaining in the grant are sufficient for the next year's studies.

We will report to you again on December 15.

Sincerely,

[redacted]

[redacted]

September 12, 1963

Dear [redacted]

Enclosed please find the accounting for [redacted] from [redacted] which shows a 0 balance. This should close that old one.

I have written to [redacted] for an accounting of the last 2 years on the $30,000 grant to the [redacted]

Enclosed is an accounting on [redacted] which I have made up since I had all his records and made the payments for him. He may use the balance up in some small expenditures which he has not yet requested reimbursement for so please don't close this one out.

Enclosed also is a copy of a letter from [redacted] which you can put in his file. He is still spending our grant money and won't account until it is all gone.

Best personal regards.

[redacted]
(When Filled In)

ACCOUNTING BY INDIVIDUAL FOR ADVANCE

SUBMITTED BY: MULTRA Sub 124

VOUCHER NO. (Finance use only):

PERIOD OF ACCOUNTING: FROM 1 October 1960 TO 31 March 1963

NOTE: Follow Instructions on Reverse

RECEIPTS

1. CASH ON HAND BEGINNING OF PERIOD		$	
1a.			
2. RECEIPT NUMBER	DATE	DESCRIPTION	
	1 Oct 1960	MULTRA Advance	
		[redacted] 14	6,500.00

TOTAL TO ACCOUNT FOR: $6,500.00

DISBURSEMENTS

3. VOUCHER NUMBER	DATE	DESCRIPTION	AMOUNT
			$
		See Attached Certification (mrb)	
		TOTAL EXPENSES	$ 3,962.21
		3a.	
		4. REFUNDED HEREWITH — CASH — CHECK — MONEY ORDER	
		5. CASH ON HAND END OF PERIOD	2,537.79
		TOTAL ACCOUNTED FOR	$ 6,500.00

I CERTIFY FUNDS ARE AVAILABLE

OBLIGATION REFERENCE NO.: 533

CHARGE ALLOTMENT NO.: 1125-1390-3902

APPROVED

DATE:

SIGNATURE OF APPROVING OFFICER: SIDNEY GUTTLIEB, DC/TSD

I certify that the expenditures listed hereon and on any attachments were incurred for official purposes of a confidential nature, that payment or credit therefor has not been received, and that this accounting is true and correct.

DATE:

SIGNATURE OF AUTHORIZING OFFICER: [redacted], mrb/hw

CERTIFIED FOR PAYMENT OR CREDIT

DATE: A

SIGNATURE OF CERTIFYING OFFICER: [redacted]

SIGNATURE OF PAYEE: [redacted] A

SPACE BELOW FOR EXCLUSIVE USE OF FINANCE DIVISION

PREPARED BY

REVIEWED BY

VOUCHER NO. 7-12

DESCRIPTION - ALL OTHER ACCOUNTS 13-33	28-33 P/A NO. / F.O. NO. / DIV.	34-39 STATION CODE / PROP. NO. / PROJECT NO.	40-42 EXPEND CODE	43 FUNDS FY	44-46 PAY PER. LIQ. CODE	47-52 OBLIG. REF. NO. / ADVANCE ACCT. NO. / EMP. NO.	53 CA	54-57 GENERAL LEDGER YR ACCT. NO.	58-67 ALLOT. OR COST ACCT. NO. / CS. NO. / X REF. NO.	68-70 DUE DATE / OBJECT CLASS	71-80 AMOUNT DEBIT	AMOUNT CREDIT
DESCRIPTION - ADVANCE ACCOUNTS 13-27												
										TOTALS		

FORM 6-61 282 USE PREVIOUS EDITIONS.

[redacted]

(1)

124-11

124

[redacted]

March 31, 1963

Grants Received

1960	$ 3,250.00	
1961	3,250.00	
		$ 6,500.00

Disbursements

[redacted] equipment & accessories		$ 2,545.06	
Mini-polygraph			
Total cost	$ 2,500.00		
Less payments by [redacted] and	1,200.00	1,300.00	
Other expense		117.15	
			3,962.21
Unexpended Balance			$ 2,537.79

This is a true statement of accounting from [redacted] reported to the Fund

I certify that services or materials have been satisfactorily received and the expenditures were incurred on official business.

[redacted]

Date: 4/9/63

124.12

RECEIPT

Receipt is hereby acknowledged of the following check:

[redacted] check [redacted] dated September 20, 1960,
in the amount of $1,426.22, drawn on the [redacted]
of th[redacted] payable to th[redacted]

[redacted]

Date: Sept 21, 1960

124-13

[redacted]

No. 533

Cost Account 1135-1009-1902

Object Class

Date	Remarks and References	Obligations Incurred	Obligations Liquidated	Unliquidated Balance
17 SEP 1960	Mkultra Sub 13	6,500.00		6,500.00

[redacted]

124-69-27

[redacted]

15 September 1960

MEMORANDUM FOR: COMPTROLLER

ATTENTION : Finance Division

SUBJECT : MKULTRA, Subproject 124

Under the authority granted in the memorandum dated 13 April 1953 from the DCI to the DD/A, and the extension of this authority in subsequent memoranda, Subproject 124 has been approved and $6,500.00 of the over-all MKULTRA project funds has been obligated to cover the subproject's expenses. This obligation of funds should be charged to Allotment 1525-1009-1902.

[redacted]
Chief
TSD/Research Branch

APPROVED FOR OBLIGATION OF FUNDS:

Original signed by
[redacted]

Research Director

Date:

I CERTIFY THAT FUNDS ARE AVAILABLE: 16 SEP 1960
OBLIGATION REFERENCE NO. 533
CHARGE TO ALLOTMENT NO. 1525-1009-1902

AUTHORIZING OFFICER

Distribution:
Orig & 2 - Addressee
1 - TSD/OC
1 - TSD/FASS

[redacted]

124-15

124

12/17 E

205640

CHEC[redacted] IN THE AMOUNT OF $3,500 00/XX

REC[redacted]

12/17 A

[redacted]
(When Filled In)

CONFIDENTIAL FUNDS POSTING VOUCHER

VOUCHER NO. 7-12 | DATE 2-6 SEP 20 1960 | VOUCHER NO. 7-12

DESCRIPTION-ALL OTHER ACCOUNTS 13-33 / DESCRIPTION-ADVANCE ACCOUNTS 13-27	28-33 T/A NO. / P.O. NO. / 32-33 DIV.	34-39 STATION CODE / PROP. NO. / PROJECT NO.	40-42 EXPEND CODE / FY	43 FUNDS	45-46 PAY PER. LIQ. CODE	47-52 OBLIG. REF. NO. / ADVANCE ACCT. NO. / EMP. NO.	53 CA YR	54-57 GENERAL LEDGER ACCT. NO.	58-67 ALLOT. OR COST ACCT. NO.	62-67 CK. NO. / X REF. NO.	68-70 DUE DATE / OBJECT CLASS	71-80 AMOUNT DEBIT	71-80 AMOUNT CREDIT
SUBPROJ 124 INV.			8811			533		601.0	25-1009-	190✓	75✓	6,500.00	
SUBPROJ 39 REFUND			88M			143		601.0	✓50✓-10-001		75✓		1,356.26
SUBPROJ 81 "			889			638		601.0	✓50✓-55-90✓		75✓		1,977.52
SUBPROJ 65 "			88M			✓664		601.0	✓50✓-10-001		75✓		50.00
SUBPROJ 88 "			889			119		601.0	✓50✓-55-90✓		75✓		1,690.00
MKULTR						45		-1100		572			1,422.22
											TOTALS	6,500.00	6,500.00

1129 SEP 20 1960

EXPLANATION OF ENTRY

See attach.

DATE	PREPARED BY	DATE	REVIEWED BY	CERTIFIED FOR PAYMENT OR CREDIT: DATE	SIGNATURE OF CERTIFYING OFFICER
19/9/60	[redacted] A				

FORM 10-59 606 USE PREVIOUS EDITIONS.

[redacted]

[redacted]

124-16

16 September 1960

MEMORANDUM FOR: CHIEF, FINANCE DIVISION

VIA : TSD/Budget Officer

SUBJECT : MKULTRA, Subproject 124, Invoice No. 1
Allotment 1125-1009-1902

1. Invoice No. 1 in the amount of $6,500 covering the above subproject is attached. However, due to refunds of $5,073.78 from other projects (as per attachments) payment should be made as follows:

Cashier's check in the amount of $1,426.22
drawn on [redacted] and made payable
to [redacted]

2. The checks should be forwarded to Chief, TSD/Research Branch, through TSD/Budget Officer, no later than Thursday, 22 September 1960.

3. This is a final invoice. However, since it is anticipated that additional funds will be obligated for this project the files should not be closed.

[redacted]
Chief
TSD/Research Branch

16 SEP 1960

I CERTIFY THAT FUNDS ARE AVAILABLE:
OBLIGATION REFERENCE No. 533
CHARGE TO ALLOTMENT No. 1125-1009-1902

AUTHORIZING OFFICER

Attachments
Invoice & Certifications

Distribution:
Orig & 2 - Addressee
1 - TSD/FASS

[redacted]

CHECK # 179194 IN THE AMOUNT OF $1,426.22
RECEIVED [redacted]

[redacted]

124-17

16 September 1960

MEMORANDUM FOR: CHIEF, FINANCE DIVISION

VIA : TSD/Budget Officer

SUBJECT : MKULTRA, Subproject 124, Invoice No. 1
Allotment 1125-1009-1902

1. Invoice No. 1 in the amount of $6,500 covering the above subproject is attached. However, due to refunds of $5,073.78 from other projects (as per attachments) payment should be made as follows:

Cashier's check in the amount of $1,426.22
drawn on a [redacted] and made payable
to the [redacted]

2. The checks should be forwarded to Chief, TSD/Research Branch, through TSD/Budget Officer, no later than Thursday, 22 September 1960.

3. This is a final invoice. However, since it is anticipated that additional funds will be obligated for this project the files should not be closed.

[redacted]
Chief
TSD/Research Branch

Attachment
Invoice & Certifications

Distribution:
Orig & 2 - Addressee
1 - TSD/FASS
XXXX
2 - TSD/RB
XXX
[redacted] (16 Sept 60)

[redacted]

[redacted]

INVOICE

For services $6,500.00

[redacted]

CERTIFICATIONS

(1) It is hereby certified that this is invoice No. 1 applying to MKULTRA, Subproject 124, that performance is satisfactory; that the services are being accomplished in accordance with mutual agreements that a detailed agenda of the payments and receipts is on file in TSD/RB, that the bill is just and correct and that payment thereof has not yet been made.

Chief, TSD/Research Branch

Date:

(2) It is hereby certified that this invoice applies to MKULTRA, Subproject 124, which was duly approved, and that the project is being carried out in accordance with the memorandum dated 13 April 1953, from the DCI to the DD/A, and the extension of this authority in subsequent memoranda.

Research Director

Date:

[redacted]

[redacted]

12-4-17

CERTIFICATION

(3) It is hereby certified that the program under subprojects 39, 81 and 65 have been satisfactorily completed and returned unused funds. However, subproject 88, which is still continuing also refunded money. Therefore, it is requested that the amounts as shown below on Invoice Number 1 of subproject 124 be credited to the subprojects as shown below.

Project	Amount	MOR	Allotment
#39	$1,356.86 OK	143	5-2502-10-001
#81	1,977.52	630	9-2502-55-902
#65	50.00	2664	8-2502-10-001
#88	1,690.00	119	9-2502-55-902
	5073.78		

Chief, TSD/Research Branch

Date:

Research Director

Date:

[redacted]

[redacted]

15 September 1960

MEMORANDUM FOR: CONTROLLER

ATTENTION : Finance Division

SUBJECT : MKULTRA, Subproject 124

Under the authority granted in the memorandum dated 13 April 1953 from the DCI to the DD/A, and the extension of this authority in subsequent memoranda, Subproject 124 has been approved and $6,500.00 of the over-all MKULTRA project funds has been obligated to cover the subproject's expenses. This obligation of funds should be charged to Allotment 1525-1009-1902.

[redacted]
Chief
TSD/Research Branch

APPROVED FOR OBLIGATION OF FUNDS:

_____
Research Director

Date: _____

Distribution:
Orig & 2 - Addressee

1 - TSD/OC
1 - TSD/FASS
1 - TSD/RB

[redacted] (15 Spt 60) [redacted]

124-19

[redacted]

A

DRAFT [redacted]
15 September 1960

MEMORANDUM FOR: THE RECORD

SUBJECT : MKULTRA, Subproject 124

1. It is requested that Subproject 124 be approved to support the research program of [redacted] in "The Psychophysiological Correlates of Carbon Dioxide Environment" in accordance with the attached proposal.

2. This study will add to our methodological sophistication for measuring carbon dioxide tension and pH of body fluids as well as our knowledge of some of the relationships between blood pH and certain psychophysiological variables mentioned in the attached proposal.

3. This project will be funded through th[redacted] for cover purposes. The accounting for funds expended shall conform to the established procedures of that organization. Title to any permanent equipment shall remain with [redacted] in lieu of overhead charges.

4. The total cost of this project for six months is estimated to be $6,500 as indicated in the attached budget. Charges should be made against Allotment 1525-1009-1902. Any unused funds will be returned to the [redacted] at the completion of the project.

[redacted]

124-1

5. [redacted]has been cleared and has served as a consultant to TSD for a number of years. He is witting of true sponsorship of the [redacted]

Sidney Gottlieb
for

[redacted] A
Chief
TSD/Research Branch

Attached:
Proposal

Distribution:
Original Only

Approved for Obligation of
Funds:

[redacted] A
Research Director

Date: 15 Sept.60

[redacted]

124-1

Downgraded to: CONFIDENTIAL
by authority of [illegible]
dated June 1977
[illegible]

[redacted]

124-19

A Proposed Study of the Psychophysiological
Correlates of the Carbon Dioxide Environment

Of all the environmental factors which influence human health, the most neglected may be one of the gaseous constituents of the atmosphere - carbon dioxide. While the proportion of carbon dioxide in fresh air runs only to 3/100 of 1%, the blood and the body cells carry a carbon dioxide tension which would be in equilibrium with an atmosphere of about 5% carbon dioxide.

Changes in the carbon dioxide tension of body fluids are related to many physiological and psychological processes. Over-breathing is one of the concomitants of anxiety. The corresponding reduction of carbon dioxide tension results in vasoconstriction and increased smooth and striated muscle tonus, with the creation of many symptoms. These symptoms may be extremely uncomfortable, and act to accentuate anxiety. This vicious circle is very difficult to interrupt, voluntarily, since breathing is largely an automatic function. We can interrupt it by increasing the carbon dioxide content of inspired air, and this is an important method of treating acute anxiety states characterized by hyperventilation.

An indication of the wide-spread applicability of carbon dioxide inhalation can be seen from two examples. Spastics and victims of Parkinson's disease may obtain appreciable relief of muscle tonus, for at least

as much as several hours, through breathing a mixture of 5-7% carbon dioxide. The mechanism is that by decreasing the pH of the blood, more body fluid calcium is ionized and this is conducive to muscle relaxation.

Another use of carbon dioxide inhalation lies in the treatment of classical migraine. In this disease, the aura phase is characterized by marked vasoconstriction of cerebral vessels which constitute part of the tree of one or the other carotid arteries. Aural phenomena, such as visual scotomata, are a reflection of temporary cerebral anoxemia. After minutes to hours of vasospasm, the affected vessels become totally exhausted and spring into vasodilation. The painful phase of migraine is thought to be an action on pain fibers in the stretched walls of the vessels. Preliminary observations indicate that inhalation of carbon dioxide in the aura phase of classical migraine can abort the syndrome by causing vasodilation before the smooth muscles of the cerebral vessels are totally exhausted.

Research in the effects of the cellular carbon dioxide environment has been negligible. This neglect may be attributable to several reasons: In the first place, accurate studies of the acid-base balance of the blood have usually required a sizeable amount of arterial blood. This is not easy to come by, since arterial puncture is a difficult and painful procedure. In the second place, there has been no simple portable device for providing carbon dioxide for inhalation. Finally, there has been no

concerted effort by pharmaceutical companies to study the problem, since no patentable drug is involved. Carbon dioxide is cheap -- omnipresent in the environment.

Long ago, one of the applicants worked on the acid-base balance with micro methods and capillary finger blood. The methods were fairly accurate but very complicated. We knew that simple methods would be perfected, but were unable to do this ourselves. In May of 1960 a simple micro system was made available in [redacted] Copenhagen

We have developed and used a simple portable source of carbogen and are presently using it in explorations of the treatment of migraine.

The situation is now ripe for a comprehensive study of the biochemical physiological, psychological and treatment aspects of alteration of the carbon dioxide level of body fluids.

It is proposed that the acid-base equilibrium of psychiatric patients be surveyed, using the new method of [redacted] Siggaard Andersen. Variations related to diagnosis and course of illness may be readily perceived. Then, with the same kind of patients, the feasibility of altering the acid-base equilibrium be carbogen inhalation, and the duration of alteration after such inhalation, would be studied on patients on normal volunteers. The effect of carbogen inhalation of selected patients, especially spastics, victims of migraine and patients with anxiety would be studied, with repeat-

X Astrup, P. Andersen, O.S. Jorgensen, K. Engel, K. "The Acid-Base Metabolism: [redacted]

A New Approach", Lancet, 14 May 1960, 1035-1039.

124-1

ed physical determinations of acid-base variables. Effect of acid-base changes on EEG, EKG and blood pressure would be determined with a polygraph which is already available.

In summary, the primary objective of the proposed study is to explore the parameters of acid-base psychophysiological correlates, using a method which has just been made available. While there are specific treatment objectives, such as in cases of excess motor tonus, migraine and anxiety, these are secondary.

2. Methods are essentially the microanalytic system of Siggaard Anderson [redacted] standard inhalation methods and a versatile polygraph. Where appropriate, psychological tests as well as psychiatric interviews would be used.

The basic facility is a very active psychiatric service specialising in acute illnesses, together with the staff and facilities of a general hospital.

3. Basic exploration should not require over 6 moths.

4. Budget. We do not yet have a breakdown on the Siggaard Anderson apparatus, but this should be available in a few weeks and will be sent in as a supplement. Total cost of apparatus is here estimated as $2,500.

Personnel:	Psychiatrist	$ 2,000 (1/3 time)
	Technician	1,500
	Apparatus	2,500
	Miscellaneous and Overhead	500
		$ 6,500

5. Qualifications: [redacted] is a large, general hospital with an active 24-bed psychiatric service. Extensive laboratory and consultative facilities are available. The Hospital is incorporated as a non-profit organization and is tax-exempt. Qualifications of the Project Director and psychiatrist are indicated below.

6. With the exception of preliminary clinical observations on the treatment of migraine, there have been no studies bearing directly on the subject of this proposal.

7. Project Director (without salary) -

[redacted]

Psychiatrist -

[redacted]

8. We have applied for a $2,000 neurological grant from the [redacted] specifically for study of treatment feasibility of classical migraine with carbogen. The present request is for basic work,

and overlap with the clinical study is minimal.

9. A rather interesting application of this study might be in the field of personality evaluation. Since there are certain psychological variables, such as anxiety, which relate to the acid-base equilibrium, it is just possible that the new and simple method of acid-base study would apply here. Possibly, the ability of an individual to withstand marked acid-base changes without development of disabling symptoms or other physical changes would be an index of psychological stability. The induction of acid-base changes, through hyperventilation, could be a kind of stress test. With the apparatus which is proposed, the extent of acid-base change could be determined readily.

The Lancet · Saturday 14 May 1960

THE ACID-BASE METABOLISM
A NEW APPROACH

POUL ASTRUP, M.D. Copenhagen
K. JØRGENSEN, M.D. Copenhagen
O. SIGGAARD ANDERSEN, M.D. Copenhagen
K. ENGEL, B.Sc. Copenhagen
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In this paper we evaluate factors which characterise disturbances of the acid-base metabolism. The importance of using chemical values, which are relevant from a clinical as well as a chemical point of view, is stressed and exemplified; and an analytical method is described for measuring the relevant chemical concentrations using capillary blood, and available as a bedside procedure.

Classification of Disturbances

The term *acidosis* should denote a pathological condition due to accumulation of acid or to loss of base. These two possibilities may lead to the same clinical picture, as both tend to lower pH in the organism. Similarly, alkalosis, or better *bassosis*, should mean a pathological condition due to accumulation of base or loss of acid.

The terms "acid" and "base" are in this paper used for hydrogen-ion donor and acceptor, respectively, according to Brønsted (1923).

The use of these widely accepted definitions increases clarity (Devoe 1953, Pratorius 1954, Relman 1954), especially because the acid-base metabolism can be dealt with independently of the cation metabolism. Cations are neither acids nor bases and should consequently not be designated bases (e.g., "total bases"), but cations.

Of all acids and bases, carbonic acid is physiologically unique because of its high endogenous production, and because its concentration is regulated by respiration. Disturbances primarily due to carbonic acid should therefore be clinically grouped separately. Accordingly, each of the two conditions—acidosis and bassosis—can be further classified as either *respiratory* or *non-respiratory*. The last group, often named "metabolic", comprises all disturbances primarily due to fixed (non-volatile) acids and bases.

Primary disturbance of the acid-base metabolism is usually compensated to some extent. A respiratory disturbance is compensated by a renal mechanism, and a non-respiratory disturbance by a respiratory mechanism. If, for instance, pH tends to fall because of an accumulation of some non-volatile acid, hyperventilation lowers the arterial pCO_2 (e.g., Kussmaul's respiration). The actual state of a pathological condition can therefore be characterised also by its degree of compensation: as *not compensated* (compensatory mechanism not working), *partially compensated* (pH not brought to normal value), *fully compensated* (pH normal), or *overcompensated*.

The terms *acidaemia* and *alkalaemia* are used in some countries for conditions in which the pH of arterial blood is decreased or increased. These terms do not interfere with the classification given here.

Estimations for Diagnosis

To indicate the severity of an acid-base disorder the following estimations have proved valuable in our experience.

Arterial blood pH depends on the relation between the respiratory and the non-respiratory components of the acid-base metabolism. It thus reflects the combined influence of respiratory and non-respiratory disturbances.

Any *deviation from the normal carbon-dioxide tension* (arterial pCO_2) reflects a *respiratory* acid-base disturbance, either primary or compensatory. This accords with the general view.

Any *deviation from the normal content of base* in blood reflects a *non-respiratory* acid-base disturbance, either primary or compensatory. The base content should be expressed as *standard bicarbonate*, or as *base excess* or *base deficit*. Standard bicarbonate is the concentration of bicarbonate in plasma, when whole blood has been equilibrated with carbon dioxide at a pCO_2 of 40 mm. Hg at 38°C, and when the haemoglobin is fully oxygenated (Jørgensen and Astrup 1957). Base excess (or base deficit) directly expresses the amount (in mEq.) of strong base (*or* acid) added per litre blood, when the normal mean is arbitrarily fixed at zero. Zero thus corresponds to the normal mean for standard bicarbonate (22·9 mEq. per litre). When the term base excess (B.E.) is used exclusively the *positive* values will express the excess of base, while the negative values will express the deficit (or base excess of acid); and this makes for simplicity in practice.

The normal 95% ranges of these values are: arterial pH 7·35–7·42; arterial pCO_2 34–45 mm. Hg; standard bicarbonate 21·3–24·8 mEq. per litre; base excess −2·3 to +2·3 mEq. per litre (Siggaard Andersen et al. 1960).

When actual values found are considered the possible diagnoses are limited, and, together with clinical information, they usually lend readily to the exact diagnosis.

Standard Bicarbonate and Base Excess

The word "standard" in standard bicarbonate should signify that the bicarbonate is measured under standard conditions in order to express only the non-respiratory side of the acid-base metabolism. The standard conditions are a fixed pCO_2 and a fixed oxygenation of haemoglobin, so that the influence of respiration on the base content of the blood is eliminated. We have chosen to measure with the haemoglobin completely oxygenated and at a pCO_2 of 40 mm. Hg and at 38°C. In with these conditions fulfilled, the pH of blood is measured, the Henderson-Hasselbalch equation

$$pH = 6{\cdot}10 + \log \frac{HCO_3^-}{pCO_2 \times 0{\cdot}030}$$

will give the standard bicarbonate directly when the value of pH found and the value of pCO_2 (40 mm.) chosen are inserted. Full oxygenation of haemoglobin is chosen for convenience, and also because it eliminates the small effect of accidental variations in oxygen saturation when venous samples are drawn. The determination of standard bicarbonate is very easy (Jørgensen and Astrup 1957).

Two other bicarbonate quantities, commonly used to indicate non-respiratory disturbances, are briefly mentioned for comparison. *Total CO_2 of plasma* is the value determined by the manometric, volumetric, or titrimetric techniques using plasma separated anaerobically from the cells. The value varies,

TABLE I—PLASMA VALUES FOR TOTAL CO_2, CO_2-COMBINING POWER, AND STANDARD BICARBONATE, DETERMINED IN SAMPLES FROM THE SAME NORMAL BLOOD POOL, AT P_{CO_2} OF 20 AND 80 MM. HG, WITH THE HAEMOGLOBIN COMPLETELY OXYGENATED AND COMPLETELY REDUCED

	Haemoglobin oxygenated		Haemoglobin reduced	
	P_{CO_2} 20 mm. Hg	P_{CO_2} 80 mm. Hg	P_{CO_2} 20 mm. Hg	P_{CO_2} 80 mm. Hg
Total CO_2 (mM.)	18·8	30·0	19·6	34·8
CO_2-combining power	18·0	28·7	21·0	31·6
Standard bicarbonate	21·2	31·3	21·2	31·2

Only the standard bicarbonate is independent of P_{CO_2} and oxygen saturation, thus showing its superiority in identifying non-respiratory disturbances

however, with the actual PCO_2 as well as with the oxygen saturation of the blood, and can therefore not be the ideal measure of non-respiratory disturbances. This is illustrated in table I.

CO_2-combining power of plasma is the total CO_2 of plasma, which is separated from the cells at the actual PCO_2 and then equilibrated at a PCO_2 of 40 mm. Hg before measurement. This value also varies with the actual PCO_2 and the oxygen saturation, though less than total CO_2 (table I).

Thus it seems evident that standard bicarbonate is the best *bicarbonate* value to measure when it is desired to eliminate the influence of the respiration and to determine the non-respiratory component only. The effect of equilibrating whole blood seems to be approximately the same in vitro as in vivo (Shock and Hastings 1935)—i.e., as if the respiratory *function* was standardized.

The standard bicarbonate value has, like other bicarbonate values, the drawback that it does not show directly the amount, in mEq. per litre blood, of fixed acid or base causing a change in the base content of a blood sample. (This is because the carbon-dioxide/bicarbonate system is responsible for only about 75% of the buffer action of the blood against fixed acids and bases, when the PCO_2 is kept constant (see table n)). Therefore, to find the total deficit or excess fix base per litre blood, the deviation of standard bicarbonate from the normal mean must be corrected; this can be approximately achieved by multiplying by 1·20. An exact correction requires knowledge of the buffer capacity of the blood—i.e., the haemoglobin concentration. The advantage of using quantities which directly give the surplus amount of fixed acids or bases contained per litre blood is thus evident. Here the use of change in buffer base or of base excess is helpful.

Buffer base (Singer and Hastings 1942), which in all cases should be used in the form agreeing with the acid-base concept of Brønsted (1923), includes buffer anions other than bicarbonate, especially haemoglobinate ions. Thereby its value becomes independent of PCO_2, and a *change* in buffer base, in mEq. per litre, directly expressed the amount of acid or base causing the change (table n). On the other hand, it represents a sum of factors of different buffer capacities. Furthermore, *the buffer base value of a blood sample depends on its haemoglobin and protein concentration* (table n). A patient with a low buffer-base value due to a low haemoglobin concentration does needs haemoglobin and not bicarbonate.

Concerning the quantity *base excess* (for definition see above), this gives directly, in mEq. per litre blood, the surplus amount of fixed acid or base (table n). It is a quantity easily understood by those unfamiliar with clinical acid-base problems. Further it allows the treatment of acid-base problems in a quantitative way. So, from both a theoretical and a practical point of view, base excess is preferable to buffer base. One argument against the use of base excess is that it does not give an ion-value for the base-concentration in blood. If this is wanted the standard bicarbonate should be used, thus giving the bicarbonate concentration of plasma under standard conditions.

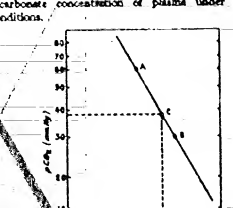

FIG. 1—nomogram for PCO_2 and pH in a blood sample.

Point A indicates the measured pH value 7·12 after equilibration at PCO_2 = 60 mm. Hg. Similarly point B indicates pH 7·36 at PCO_2 = 50 mm. Hg. If, for instance, the actual pH of the metabolically drawn blood had been measured to 7·24, the actual PCO_2 would be read as 56 mm. Hg (point C).

Total CO_2, CO_2-combining power, standard bicarbonate, buffer base, and base excess can be determined by the new microtechnique outlined below.

Quantitative Treatment of Acid-base Disturbances

Respiratory Disturbances

Changes in the alveolar ventilation, leading to respiratory disturbances, are determined quantitatively by the PCO_2 of arterial blood, the value of which in general can be assumed to be identical with the value of PCO_2 of alveolar air.

As the excreted amount of carbon dioxide per time unit is constant for an individual in a steady state, the

TABLE II—VALUES FOR BUFFER BASE, BASE EXCESS, AND STANDARD BICARBONATE, DETERMINED IN BLOOD SAMPLES WITH DIFFERENT CONCENTRATIONS OF HAEMOGLOBIN (15 AND 7·5 G. PER 100 ML.) AND WITH OR WITHOUT ADDITION OF STRONG ACID AND BASE (10 mEq. PER LITRE BLOOD)

	Blood with 15 g. haemoglobin per 100 ml.			Blood with 7·5 g. haemoglobin per 100 ml.		
	No acid or base added	10 mEq. strong acid added per litre blood	10 mEq. strong base added per litre blood	No acid or base added	10 mEq. strong acid added per litre blood	10 mEq. strong base added per litre blood
Buffer base (mEq. per litre blood)	46·2	36·2	56·2	43·4	33·4	53·4
Base excess (mEq. per litre blood)	0	−10	+10	0	−10	+10
Standard bicarbonate (mEq. per litre plasma)	22·9	15·9	30·7	22·4	15·4	31·4

The blood samples were obtained from a pool of normal blood kept at 38°C, at PCO_2 = 40 mm. Hg, and with the haemoglobin completely oxygenated. The haemoglobin concentration was altered by adding plasma.

product of the alveolar ventilation (A) and the pCO_2 of the arterial blood has a constant value (K): $A \times pCO_2 = K$. Accordingly, if the alveolar ventilation decreases, the pCO_2 must increase, and vice versa. For instance, a decrease of A to half must double the pCO_2.

In some cases additional laboratory measurements help in elucidating the cause of a respiratory disturbance. Among these the measurement of the oxygen saturation or the oxygen tension (pO_2) of arterial blood is important. Thus, a low oxygen saturation with a low pCO_2 is associated with completely different diseases to a low oxygen saturation with a high pCO_2.

Non-respiratory Disturbances

When dealing with the *non-respiratory disturbances*, knowledge of the total amount of excess acid or base in the organism can be of clinical importance. The problems involved are rather complex, and for proper treatment knowledge of the distribution of acid and base in the different body-spaces and the rate of exchange between them is required. The following approximations are helpful.

The deficit or excess of base in *the extracellular body-space* can be estimated in mEq. by multiplying the negative

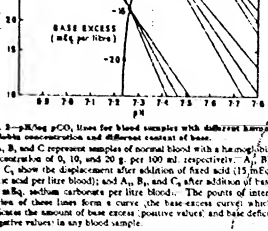

Fig. 3—pH/log pCO_2 lines for blood samples with different haemoglobin concentration and different content of base.

A, B, and C represent samples of normal blood with a haemoglobin concentration of 0, 10, and 20 g. per 100 ml. respectively. A_1, B_1, and C_1 show the displacement after addition of fixed acid (15 mEq. acetic acid per litre blood); and A_2, B_2, and C_2 after addition of base (15 mEq. sodium carbonate per litre blood). The points of intersection of these lines form a curve (the base excess curve) which indicates the amount of base excess (positive values) and base deficit (negative values) in any blood sample.

or positive value found for base excess, in mEq. per litre blood, by 0·3 × the body-weight in kg., where the factor 0·3 is found experimentally (Mellemgaard and Astrup 1960). This amount corresponds directly to the amount of sodium bicarbonate or of ammonium chloride required to neutralise a non-respiratory disturbance in the *extracellular space*.

For *the whole body*, the factor 0·7 should be used instead of 0·3 (Palmer and Van Slyke 1917).

In dealing with patients, however, the amount of excess or deficit of base in the whole body does not always seem to be directly proportional to the excess or deficit of base in the

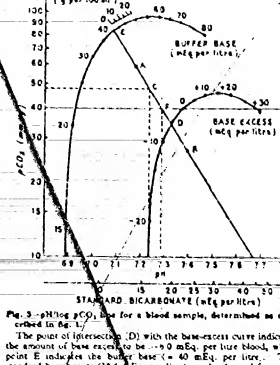

Fig. 3—pH/log pCO_2 lines for a blood sample, determined as described in fig. 1.

The point of intersection (D) with the base-excess curve indicates the amount of base excess to be −9·0 mEq. per litre blood, while point E indicates the buffer base (= 40 mEq. per litre). The standard bicarbonate (18·6 mEq. per litre) can be derived from the pH value corresponding to a pCO_2 = 40 mm. Hg (F).

The absolute shown pH values and standard bicarbonate. The total CO_2 of the plasma from the anaerobically drawn blood and the CO_2-combining power can be found from the figure. (For the calculation see Siggaard-Andersen and Engel 1960).

blood. When, therefore, patients are to be treated with intravenous infusions of acid or base, it is advisable to estimate the dose necessary to normalise the base content of the extracellular space only, and then follow the effect of the treatment by frequent blood analyses and also by clinical observation, before new infusions are given. Thus overtreatment is avoided (Mellemgaard and Astrup 1960).

In treating the non-respiratory disturbances, it is important to estimate an abnormal loss of acid or base. This is especially so when the loss is extrarenal—e.g., in

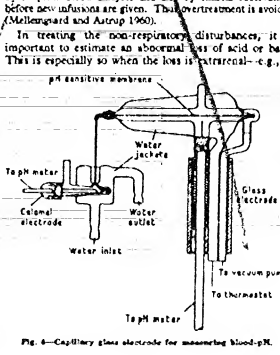

Fig. 4—Capillary glass electrode for measuring blood-pH.

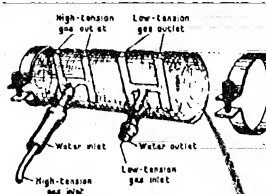

Fig. 6—Chamber for simultaneous equilibration of micro-samples in duplicate at two different carbon-dioxide tensions.

pyloric stenosis and pancreatic fistula. In such cases the lost amount of acid or base should be determined by titration together with the twenty-four-hour excretion of acid or base in urine (Jørgensen 1957).

Micromethod for Determining pH, pCO_2, Standard Bicarbonate, and Base Excess

When using macromethods for determining the above relevant values for characterising the acid-base status, arterial punctures are necessary. This is a drawback when frequent analyses are needed—for instance at intervals of minutes in cases with rapid changes in the respiration (in anæsthesiology, treatment in a respirator, &c.). A micromethod, using about 100 µl. blood, was therefore developed (Siggaard Andersen et al. 1960).

Principle

The theoretical background for the calculation of pCO_2, standard bicarbonate, and base excess is that graphs showing the relations between pH and pCO_2 and between pH and pCO_2 are approximately straight lines (shown experimentally by Brewin et al. 1958 and Astrup 1956). The slope of the lines depends on the buffer capacity of the blood. By equilibrating a blood sample at two known pCO_2 tensions and measuring the pH values, the line for the sample is determined (fig. 1). If the actual pH of the blood sample is known, then the actual pCO_2 can easily be found.

When fixed acid is added to the blood, the line is displaced to the left. When base is added, the line is displaced to the right. Now a graph (fig. 2) can be constructed expressing the displacement caused by any amount of acid or base, independent of the hæmoglobin concentration (Siggaard Andersen and Engel 1960).

The point of intersection between this curve and a found pH/log pCO_2 line for a blood sample thus indicates, in mEq./l., the base excess per litre blood.

In the same diagram a curve can be constructed (Siggaard Andersen and Engel 1960) expressing the content of buffer base according to the definition of Singer and Hastings (1948). The curve is shown in the upper left corner in fig. 3. By using this curve the amount of buffer base in blood can be found.

Thus exact measurement of blood pH at the actual pCO_2 and at two known values for pCO_2 will allow the calculation of all relevant blood data concerning the acid-base status. This is illustrated in fig. 3.

Equipment for Determination at Bedside

The equipment is described in detail elsewhere (Siggaard Andersen, et al. 1960). It consists of a pH-meter, a circulating thermostat, a suction pump, a micro-electrode (fig. 4) according to Saxa (1957), and a micro-equilibration chamber (fig. 5). All these parts can be mounted on a portable table together with two small cylinders containing mixtures of oxygen and carbon dioxide.

Capillary blood is drawn from ear or finger. For the actual pH about 20–25 µl. is sucked directly into the capillary electrode (the principle of Saxa 1957) and the reading is made immediately, or it is sucked from blood drawn anaerobically into a heparinised capillary glass tube with sodium fluoride). About 80–90 µl. of blood from two capillary glass tubes is divided between two of the chambers in the equilibration apparatus. This is then shaken mechanically (2600 r.p.m.) and after three minutes the pH values in the two samples are measured successively. By using these two values and the corresponding pCO_2 values (from the cylinders), the pH/log pCO_2 line is drawn and the pCO_2, standard bicarbonate, and base excess can be calculated (fig. 3). The method is

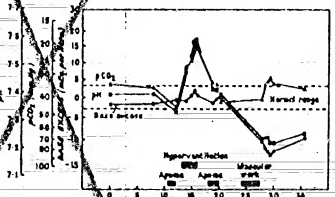

Fig. 7—Case 2: values for pH, pCO_2, and base excess of blood from a normal person during a short period of maximal hyperventilation, apnoea as long as possible, and horizontal work on a cycle ergometer.

The ordinate shows pH, pCO_2, and base excess, the abscissa time in minutes.

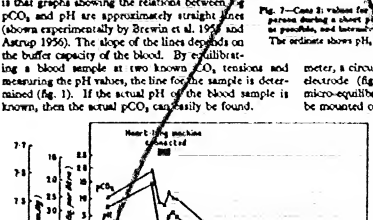

Fig. 8—Case 1: values for pH, pCO_2, and base excess of blood from a patient operated on for a dissect in the atrial septum.

The ordinate shows pH, pCO_2, and base excess, the abscissa time in hours. For further explanation see text.

highly accurate, as the three values can be found with an error of less than ± 2

Illustrative Cases

The advantage of frequent registration of pH, pCO_2, and base excess by the method described here is illustrated in the following two cases. Figs. 6 and 7 show a convenient graphic system for these three quantities.

Case 1.—Fig. 6 shows blood values from a patient (female, 15 years old, operated on for a defect in the atrial septum. At the beginning of the operation the values for the non-respiratory component indicate a slight base deficit, possibly due to the postabsorptive phase. A manifest non-respiratory acidosis develops as soon as the blood of the patient is mixed with the rather acid donor blood from the heart-lung machine (approximately 4 litres with a base excess of − 12 mEq. per litre, mainly due to lactic acid). The acid excess quickly decreases, partly by distribution between the different body compartments, and partly by oxidation of the lactic acid. The second day after the operation a normal value is reached.

The curve for the respiratory component (pCO_2) shows first the effect of overventilation during the anæsthesia. A slight rise in pCO_2 is seen when the heart-lung machine is responsible for the CO_2 excretion. When spontaneous respiration was established after the operation the pCO_2 was between 50 and 60 mm. Hg, reaching a normal value within a few hours.

The pH curve shows the resulting action of the respiratory and non-respiratory components on the hydrogen-ion concentration.

Case 2.—The pronounced deviations from normal acid-base values seen in a normal individual (male 26 years old) by maximal hyperventilation, periods of apnœa, and intensive muscular exercise of short duration are illustrated in fig. 7.

The rise in pCO_2 and the fall in pH during the two apnœa periods are moderate and obviously the fall in oxygen saturation (to about 80%, not measured accurately) is the limiting factor for the length of voluntary suspension of breath. During hyperventilation a fall in pCO_2 to about 20 mm. Hg was observed. The muscular exercise was followed by enormous hyperventilation, but the pCO_2 was now practically within normal limits. The explanation must be that the greatly increased CO_2 production is compensated by an equally increased CO_2 excretion by means of the hyperventilation.

Only small variations, within the normal limits, are seen during the pure respiratory changes. A possible cause of these small variations is displacement of base between the different body-spaces; this point deserves further investigation. During the muscular exercise a heavy non-respiratory acidosis develops, with a base excess of − 12 mEq. per litre, indicating accumulation of large amounts of lactic acid.

Great fluctuation in the pH from 7·58 and 7·21, observed over a period of ten to fifteen minutes, was caused exclusively by a fall in pCO_2 and in base excess.

Summary

Disturbances in the acid-base metabolism have been classified according to the relation between blood values for pH, pCO_2, and an index of non-respiratory disturbances. This index should be either bicarbonate concentration measured under standard conditions as "standard bicarbonate" or else the surplus amount, as "base excess", of fixed acid or base in mEq. per litre blood. Knowledge of the value of base excess enables the total deficit or excess of base in the blood-volume and in the extracellular space to be calculated.

An accurate bedside method, using capillary blood, for determining all relevant blood values for the identification of disturbances in the acid-base metabolism, qualitatively and quantitatively, has been devised.

References at foot of next column

MEDICAL ASPECTS OF ROAD SAFETY *

L. G. Norman
M.D., B.Sc. Lond., M.R.C.P., D.P.H.
CHIEF MEDICAL OFFICER, LONDON TRANSPORT EXECUTIVE

To drive safely requires the use of certain physical and mental qualities in reasonable degree. But these qualities can seldom be precisely defined and they cannot be quantified. Perhaps the nature and amount of the eyesight required for driving have been more fully established than those of other qualities, but even here the borderline between fitness and unfitness to drive is somewhat arbitrary.

In Great Britain in 1958 the police reported 992 road accidents in which a driver was ill or in which his physical defect was regarded as a contributory cause (Road Accidents 1958). This is a small proportion of the total number of accidents, but their prevention is of particular medical interest.

The clinical assessment of fitness to drive does not involve the development of yet another branch of Medicine. It is simply the application of clinical knowledge to the particular requirement of driving vehicles safely; and, as almost all doctors drive themselves, they are in the fortunate—and unusual—position of having practical experience of both sides of this question. Many adult patients are drivers who may seek advice on their fitness to drive during convalescence or in relation to chronic disease. This is especially important for professional drivers who may be responsible for the safety of many passengers.

A general guide for physicians on the assessment of fitness to drive has been published by the American Medical Association (1959) which has also produced a bright little booklet for patients, entitled "Are You Fit to Drive?". The British Medical Association (1954) and the World Health Organisation (1956) have also published helpful guides for physicians. These are not as well known as they should be.

In assessing the fitness of drivers it is usual to consider three types of vehicle: (1) the public-service vehicle in which seventy or more passengers may be carried, (2) the heavy commercial vehicle, and (3) the private car. The driver of public-service and commercial vehicles is a professional who generally drives for several hours a day; the private-car driver is usually an amateur whose driving may be for as little as half an hour a week or as much as eight hours a day—for example, some sales representatives. The risk of accident due to a medical condition in a driver increases with the time he spends driving. Hence, in assessing the fitness of patients to

* The second Milroy lecture for 1960, delivered before the Royal College of Physicians of London on Feb. 4. The first lecture appeared last week.

DR. ASTRUP & OTHERS: REFERENCES

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[redacted]

26 August 1960

MEMORANDUM FOR: THE RECORD

SUBJECT : Approval of [redacted] Study of the "Psychophysiological Correlates of the Carbon Dioxide Environment."

ATTENDANCE : [redacted] Cottlieb [redacted]

SUMMARY: 1. Request for $6,500 to carry out [redacted] study was approved. It was recognized that this is primarily a technique study as proposed but that, once [redacted] became familiar with the apparatus, a tighter design could be developed. [redacted] agreed to work with [redacted] when the time was propitious.

2. Funding will be effected through the [redacted] mechanism. [redacted] to permanent equipment will remain with [redacted]

[redacted]

TSD/Research Branch

Distribution:
Orig & 3 - TSD/RB

	Rec'd.	Fwd.
A [redacted]	HWB	9/19
	SG	8 Sept
	JWG	27 Sept
	DAR	28 Sept 60

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TSD/RB

Date Recd		Date Fwd
8/22	[redacted]	8/22
8/23		8/23
22 Aug		23 Aug
23 VIII		23 VIII

Remarks Meeting - 1400

Friday, 26 August 1960

FILE

[redacted]

[redacted] B

DEPARTMENT OF MEDICINE

July 18, 1960

[redacted] C

Re: "A Proposed Study of the Psychophysiological Correlates of the Carbon Dioxide Environment" by [redacted] C

Dear [redacted] C

I have reviewed this request carefully. It is really very interesting for me to see how methods for the analysis of blood CO_2, pH, etc. are becoming increasingly available for use at the bedside, and I am also happy to see that people such as [redacted] are interested in using these methods to study man's reactions in real life situations. However, I am not at all happy about the hypothesis that they are putting forward for their proposed research. This hypothesis seems to come in that category of, "Let's study a group of patients and see if they aren't abnormal with regard to this or that." There are so many things that can cause the acid-base equilibrium of people who change rapidly over short periods of time that, no matter what was found in a survey of psychiatric patients as compared to normals, it would be unlikely that one could draw any conclusions from the findings which would help one understand the role of the intracellular CO_2 in various forms of psychiatric disease. My suggestion then is that these investigators have good methods but that their hypothesis and experimental design leave something to be desired.

I would suggest that we devote the sums available for work in this area to some projects that are different, but maintain an open mind about these investigators.

Sincerely,

[redacted] C

[redacted]

124-24

[redacted]

June 24, 1960

[redacted]

Dear [redacted]

Herewith is a proposal for investigation of the psychophysiological correlates of the carbon dioxide environment. I hope that you will find it interesting.

I am enclosing a single reprint of the study which I did with [redacted] 1936, which is referred to in the application, together with a photocopy of the recent report from Copenhagen on simplified methods for studying the acid-base equilibrium.

Sincerely,

[redacted]

Approved for Hospital Administrator

[redacted]

[redacted]

[redacted]

INVOICE CHECK LIST

MKULTRA Subproject

At Date of Original Authorization	Period Covered	Time Extended To	Allotment Number	Amount of Obligation
15 Sept 1960				6,500

Additional Authorizations	Period Covered	Time Extended To	Allotment Number	Amount of Obligation
#1				-0-

Invoice Number	Date	Amount	Balance
#1	16 Sept 1960	5073.78 1426.22	-0-
REMARKS:			

[redacted]